occur without irradiation.[9,15] Anaplastic shift bears a grim prognosis, and the majority of patients die within one year of its detection.[14-16] In two of our patients, a change in the size of metastatic nodules that had been stable for 15 to 17 years heralded an anaplastic shift—an occurrence that has not been previously reported. Although such growths can occur without a change in the histologic appearance of the tumor, we believe that rapid enlargement of pulmonary lesions in a patient with previously stable metastasis suggests the presence of anaplastic shift and indicates the need for biopsy.

Respiratory symptoms are uncommon in patients with thyroid carcinoma that metastasizes to the lungs. Only one patient in our group was symptomatic at the time pulmonary metastases were detected; dyspnea on extertion was his only complaint. During his illness this patient developed polycythemia that was due to hypoxemia resulting from pulmonary arteriovenous shunting within highly vascular metastases. This arteriovenous shunting is known to occur in patients with metastatic thyroid carcinoma,[5] and an identical case, with angiographic confirmation, was reported by McGee and Warren.[4] In such patients, innumerable nodular densities appear on x-ray films of the chest. Probably, diffuse pulmonary metastases are necessary to produce shunting of such a magnitude that arterial oxygen desaturation and polycythemia will result.

Summary

This report presents four cases with the uncommon finding of unchanging pulmonary nodules due to metastatic papillary thyroid carcinoma. Radiographic follow-up periods ranged from 14 to 25 years. Three patients were less than 40 years of age at the time of first diagnosis; this reflects the good prognosis for young people with this disease. Three patients were initially asymptomatic, but the fourth had dyspnea that probably resulted from pulmonary arteriovenous shunting associated with miliary metastases. Rapid growth of previously stable metastatic nodules in two patients suggests anaplastic shift, and this finding may indicate the need for lung biopsy.

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Disposition of Acetone Following Acute Acetone Intoxication

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ALTHOUGH ACETONE is a component of a large variety of industrial and household cleaners, glues and solvents, acute acetone intoxication has not been frequently reported.[1,2] Acetone is relatively nontoxic; ingestion of as much as 200 to 400 ml may not result in serious sequelae.[3,4] Symptoms of mild acetone intoxication are characterized by drowsiness and incoherent speech,[1,2] while in more severe cases stupor and deep coma may result. Since acetone is excreted by the lungs, the odor of acetone is always found on the patient's breath. The effects of acetone are said to be similar to those of ethanol at equal blood levels, although the anesthetic potency is greater.[5] There is little information about the kinetics of the disappearance of acetone in persons following

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acute oral ingestion.[4,5] In this report we describe the clinical symptoms and the kinetics of elimination of acetone in a patient who presented on two occasions with acute acetone intoxication.

Report of a Case

A 53-year-old woman was brought to the emergency room after her sister found her in a lethargic, minimally responsive state. During the previous week, neighbors had noted that she seemed increasingly lethargic and unsteady. She had had multiple previous medical and psychiatric admission for acute and chronic alcohol abuse. Pertinent medical history included biopsy-proven Laennec cirrhosis and a history of a portacaval shunt done 13 years earlier for upper gastrointestinal bleeding presumed to be secondary to varices. Other complications of alcoholism included a peripheral neuropathy and cerebellar atrophy as well as alcoholic withdrawal seizures. Two years before this admission she had suffered a cerebrovascular occlusion resulting in temporary aphasia and a residual right-sided weakness, and she required a cane for ambulation. Her medications at the time of admission were phenytoin and phenobarbital for seizure control and furosemide and potassium chloride for mild hypertension. At the time of physical examination she appeared as a tremulous female who had a fruity odor on her breath and a tendency to pick frequently at her hair. Her vital signs were normal. The oral mucosa showed no ulceration or injection. Results of chest and cardiac examination were unremarkable. Abdominal examination revealed a liver with a span of approximately 10 cm. Other findings of the general physical examination were essentially within normal limits. Neurological examination showed that the patient was oriented, lethargic but arousable, and had a shortened attention span. She was able to follow simple commands. Cranial nerves were intact and reflexes were symmetric with no pathological reflexes. Gait was broad-based but otherwise motor and sensory examination showed no gross abnormalities. Analysis of urine revealed a specific gravity of 1.017 and a 3+ value for ketones but no glucose. Arterial blood gas studies showed a pH of 7.51, arterial oxygen pressure (Pao_2) of 81 mm of mercury and arterial carbon dioxide pressure ($Paco_2$) of 27 mm of mercury. Toxicology screening of blood showed a phenytoin level of less than 2.5 μg per ml, a phenobarbital level of 15 μg per ml, and an acetone concentration of 0.25 gram per dl, measured by gas chromatography. The blood ethanol and isopropanol levels were zero. Acetone was detectable in material obtained from a gastric aspiration. The patient was admitted for observation, and over the next 72 hours she demonstrated slowly progressive improvement in her level of consciousness. Subsequently, a half-empty bottle of nail-polish remover was found in the patient's home but she denied ingesting its contents.

Approximately a month later, the patient was again brought to the emergency room with a one-day history of increasing lethargy and somnolence. Results of physical and laboratory examinations were similar to those from the previous admission. Toxicology examination again revealed a blood acetone concentration of 0.25 gram per dl. The patient was admitted for observation and showed gradual improvement in her mental status as acetone levels declined (see Figure 1). After five days she was transferred to an alcoholic rehabilitation center for long-term control and management of her alcohol problem.

Discussion

A definite history of acetone ingestion could not be obtained from this patient on either of her two admissions. Detectable concentrations of acetone in the blood may be observed in several other clinical settings. In diabetic ketoacidosis, for example, the range of acetone concentrations found is approximately 0.01 to 0.07 gram per dl.[4,6] In isopropyl alcohol intoxication, acetone concentrations in plasma and breath may be measured due to the metabolic conversion of isopropyl alcohol to acetone. However, the high concentration of acetone observed in this patient could have resulted only from the direct ingestion of acetone. Two reported signs of acute acetone ingestion are a red and swollen pharynx and erosions of the soft palate. These were not seen in this patient, and it is likely that the acetone was diluted in another liquid and taken over a period of time. This reconstruction is supported by the gradual development of symptoms on both occasions over a period of several days.

Surprisingly few data are available regarding the human rate of elimination of acetone, particularly at the high blood levels seen in intoxicated patients. Haggard and co-workers[5] studied volunteers who drank as much as 80 mg per kg of body weight of acetone; they found that the maximal concentration of acetone in blood was

about 0.007 gram per dl. They calculated that, at this concentration, 70 percent of the total elimination of acetone was due to metabolic conversion and that the fraction of elimination due to metabolism increases as the concentration falls. These data of Haggard and those of DiVincenzo[7] indicate nonlinear and saturable metabolism of acetone at concentrations much lower than those seen in patients with acute acetone intoxication.

Saturable metabolism of acetone has also been documented in rats, with a zero-order elimination rate of 13 mg per kg of body weight per hour being reached at a concentration of 0.2 gram per dl.[5] The maximum rate of metabolism in humans is not known, but comparison of the human data[5] with the data in rats at similar concentrations suggests that the maximum metabolic rate on a weight basis would be lower in humans. For a patient of average size, metabolic conversion of acetone probably cannot exceed 1 gram per hour.

The volume of distribution of acetone (which is a measure of the fraction of drug in the body that is found in the blood) is estimated to be about

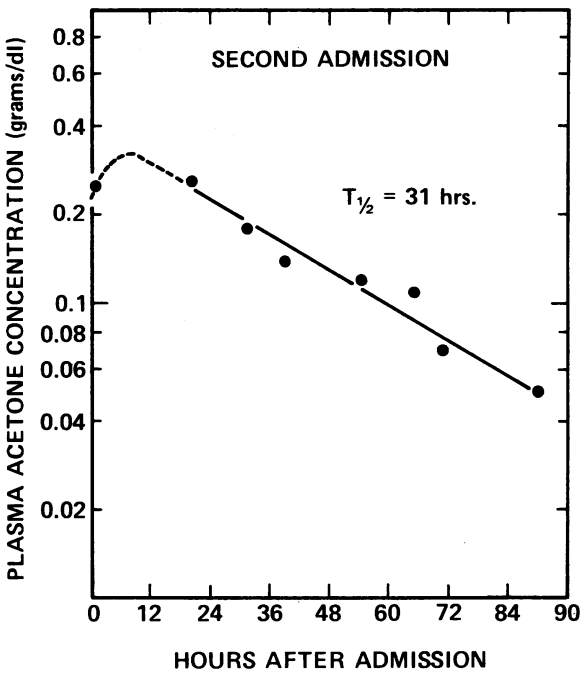

Figure 1.—Time course of acetone concentrations in blood following the second admission for acetone intoxication. The half-life, calculated by nonlinear least squares regression analysis of the data from 19 hours after admission and beyond, is 31 hours. This is similar to a half-life of 28 hours calculated on the first admission with fewer data points. Although there is considerable scatter in the data, they appear to be log-linear and consistent with a first-order elimination process.

0.82 liter per kg or 82 percent of body weight, which is approximately equal to total body water.[5] Based on a concentration of acetone of 0.25 gram per dl at the time of admission, it can be estimated this patient had about 150 grams of acetone in her body. Allowing for some possible continued absorption during the first several hours after admission, the disappearance of acetone from blood appears to follow a log-linear (or first-order) pattern, with a half-life of 31 hours, as calculated by the nonlinear regression program MLAB (Modeling Laboratory).[8] During the 19-hour interval between the collection of the second and fourth acetone samples, roughly 75 grams of acetone were eliminated from her body, well in excess of the 19 grams that could be due to metabolic conversion of acetone. Urinary excretion of acetone is minimal; the patient's urine/blood concentration ratio for acetone was found to be 1.08, similar in magnitude to that reported by others.[5,9]

The remaining, and most important, route of elimination of acetone in the acutely intoxicated patient is therefore the respiratory tract. Haggard and co-workers[5] and Briggs and Schaffer[9] have found that the concentration ratio of acetone in blood/alveolar air is 330. This means that 330 liters of alveolar air must be exchanged to "clear" the acetone from 1 liter of blood. Using an average minute ventilation of 9.65 liters per minute based on this patient's age, weight and sex,[10] the clearance of acetone by the lungs can be calculated to be 29 ml per minute, or 0.39 ml per minute per kg of body weight. With a volume of distribution of 0.82 liter per kg of body weight, the half-life would be expected to be 25 hours. This figure is in reasonable agreement with the half-life observed in this patient. The extent to which this patient's liver disease contributed to the long half-life cannot be assessed, but it is probably minor, considering the low concentrations at which metabolism is saturated in subjects with normal liver function.

It is apparent from the above discussion that at concentration above 0.1 gram per dl, the rate of elimination of acetone is determined by the respiratory execretion rate. The pulmonary clearance, however, is low; and thus the half-life of acetone is relatively long, more than 30 hours in this patient. Theoretically, one might increase the pulmonary clearance by means of hyperventilation, but the toxicity of acetone is so low that

this approach would probably not be frequently justified. As with this patient, improvement is gradual and follows a time course similar to the decline seen in blood acetone concentrations. Clinically, it is important to recognize that the time required for recovery of these patients is measured in days, and that acetone concentrations may be useful in distinguishing acetone intoxication from other causes of central nervous system depression.

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Pancreatitis as the Presenting Manifestation of Miliary Tuberculosis

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THE CLINICAL PRESENTATION of miliary tuberculosis may take many forms. Some of these are quite nonspecific and obscure,[1-3] making the diagnosis very difficult at times. Although not widely appreciated, it is not uncommon for abdominal pain to be a major clinical finding. This has been attributed largely to tuberculous infiltration of the peritoneum and gastrointestinal tract.[2,4] Pancreatitis and hyperamylasemia, however, are exceedingly rare features of miliary tuberculosis[5,6] and neither has been previously reported as a presenting feature of this disease.

The association of the adult respiratory distress syndrome (ARDS) and miliary tuberculosis is also an uncommon occurrence. Only six cases have been reported.[7-10] We recently cared for a patient in whom both pancreatitis and a transient episode of ARDS developed as complications of miliary tuberculosis. Because each of these conditions is a distinctly unusual feature of disseminated tuberculosis infections, we wish to report our experience.

Report of a Case

The patient was a 39-year-old black man admitted with a three-week history of intermittent right upper quadrant abdominal pain and a one-week history of fever, malaise, nausea and vomiting.

The patient said that he did not use alcohol, did not smoke and had not been exposed to tuberculosis. He was told he had sarcoidosis at another hospital seven years previously—the diagnosis based on abnormal findings on a roentgenogram of the chest. No further studies were carried out, and he was not treated. His past history was otherwise noncontributory.

On physical examination at admission the patient was noted to be well-developed and thin; body temperature was 39.4°C (103°F). Mild epigastric tenderness was elicited by palpation; neither organomegaly nor rebound tenderness was present. The other findings from the examination were noncontributory.

A roentgenogram of the chest done at admission (Figure 1) showed bilateral hilar and right paratracheal lymph node enlargement. An electrocardiogram showed no abnormalities. A complete blood count gave the following values: hemoglobin, 14.2 grams per dl; hematocrit, 41.4 percent; leukocyte count, 4,800, with 19 percent bands, 52 percent polymorphonuclear cells, 17 percent lymphocytes and 12 percent monocytes. Analysis of urine showed 1+ protein by dipstick and up to two leukocytes per high-power field; other results were within normal limits. Electrolytes and blood urea nitrogen were normal, as were the prothrombin and partial thromboplastin times. The serum glutamic-oxaloacetic transami-

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